CLINICAL RESEARCH STUDIES

From the Southern Association for Vascular Surgery

Presidential address: A brief history of arterial blood flow—from Harvey and Newton to computational analysis

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My education and interests have always pointed toward fluid mechanics both as a researcher and as a clinical vascular surgeon trying to restore or maintain arterial blood flow. In 1970 to 1971 I was a research fellow at the Cardiovascular Research Institute of the University of California Medical Center, San Francisco. The director of the Institute, Julius Comroe, wrote a small book entitled *Retrospectroscope: Insights Into Medical Discovery*,[1] in which he makes a strong case for basic science research leading to unexpected important findings, as opposed to targeted research. The first correct description of human circulation was given almost 400 years ago by William Harvey. During this same period the laws that govern physical science in general and blood flow in particular were formulated mathematically by Isaac Newton. My retrospectroscope is a brief history of the basis of and advances in our knowledge of arterial blood flow from the time of Harvey and Newton to the present. Fundamental discoveries centuries ago have come full circle to contribute to current vascular surgical knowledge and research.

In the past few decades there have been major advancements in unraveling the complexities of vascular biology. Understanding of the intricate characteristics of arterial blood flow and the way in which they interact with and contribute to vascular diseases is rapidly evolving. During the 25-year history of this society there have been major advances in vascular surgery. At the same time there has been revolutionary progress in solving complex problems involving the analysis, design, and optimization both of solid bodies moving through fluids, such as aircraft and ships, and of fluids moving through vessels, like arterial blood flow. The basis of solving these problems lies in accurately determining fluid flow patterns near solid walls. These problems are defined by physical laws represented by differential equations that have been known for centuries. Computational analysis, a numerical method of solving these equations, was developed years ago, awaiting the advent of high-speed computers to do the work.

When pulsatile flow in an arterial segment is smooth and undisturbed, the probability of myointimal hyperplasia, thrombosis, or atherosclerosis developing is low. The converse is true in segments that have disturbed flow. These adverse hemodynamics are characterized by recirculation zones, flow separation and reattachment, vortex propagation, and prolonged near-wall blood particle residence times. Disturbed flows or nonuniform hemodynamics produce both abnormally high and low arterial wall shear stresses and high wall shear stress gradients. These stresses may trigger a cascade of adverse biological events in the arterial wall that may lead to the local development of myointimal hyperplasia, new or recurrent atherosclerosis, or thrombus formation. Although systemic risk factors are involved in the development of arterial diseases, local flow-induced arterial wall forces also play a major role. With the advent of arterial repair, endarterectomy, bypass grafts, and angioplasty and stenting we as vascular surgeons have some control over arterial geometry and therefore the way in which blood flows through them. Optimizing hemodynamics through design of arterial reconstructions is a realistic and valid application of the principles of fluid mechanics. Predicting native arteries at risk for developing atherosclerosis because of their geometric-induced adverse hemodynamics is a potentially useful application of blood flow analysis.

THE 17TH CENTURY: HARVEY AND NEWTON.

William Harvey (1578-1657) was educated in astronomy, mathematics, biology, and medicine at Padua. While Harvey was a student there, Galileo was the professor of astronomy. However, it is unclear what influence he had on

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Competition of interest: nil.

J Vasc Surg 2001;34:398-404.

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0741-5214/2001/$35.00 + 0 **24/6/116108**

doi:10.1067/mva.2001.116108

Harvey.[2] Galileo was a proponent of the Copernican system of the universe, which held that the planets were in circular orbits about the sun. This concept was at odds with church doctrine that our planet was the center of the universe. Being within Rome's jurisdiction, Galileo was twice taken before the Inquisition and accused of heresy. He acquiesced both times, publicly renouncing Copernicanism. William Harvey fared much better after returning home. England was free from church dogma, and with the resumption of the acceptance of human dissection he turned his attention to physiologic deductions that were based on anatomic studies. In 1616 at the age of 38 he delivered a lecture to the College of Physicians in London in which he described the circulation to be driven by the heart with blood flowing from the arteries to the veins in a "circular" manner.[3] He deduced this in part from his observation that venous valves open toward the heart. This correct concept of the circulation was quite different from the Galen principle that had been accepted for more than 1400 years. Blood was thought to be produced in the liver and travel to the various organs and tissues through the veins where it was used in some way, but not recirculated. Harvey postulated that there were porosities in both the lungs and the systemic tissues that allowed passage of blood. Capillary beds were described and microscopically confirmed after his death. On the basis of anatomical studies of the human heart chamber size and heart rate, he estimated resting cardiac output to be approximately 4 L/min, low but amazingly close.

Harvey had no idea of the function of the lungs. It would be another 50 years before Robert Boyle discovered that lungs oxygenated blood and that oxygen was necessary to support life. The ancient Greeks recognized that air was vital to life but thought that arteries carried air and veins carried blood. This concept remained until Harvey's discoveries. A century before Harvey, Michael Servetus, a physician and Christian theologian, demonstrated the change in color of blood from dark to bright red when it traversed the lungs. However, no one acted on this information for more than a century, almost surely because it was in conflict with the Galen principle and church doctrine. At the age of 42, Servetus was convicted by the Inquisition and burned at the stake.[3]

Isaac Newton (1642-1737) published his monumental work *The Principia Mathematica* in 1684 at the age of 44.[4] This culmination of more than 20 years of work set down the physical laws of motion, gravity, and force that govern the universe. He introduced the modern scientific method based on inductive reasoning, which states that a general theory or postulate based on observed facts can be proven to be a law if it also explains related phenomenon. Most historians agree that the *Principia* was the single most important work ever published in the physical sciences. It changed the way scientists thought and ushered in the modern world. The foundation of physical science was set only to be slightly tweaked more than two centuries later by Einstein's relativity theory. Although Galileo's and other's experimental observations of the orbits of planets and the paths of falling bodies paved the way for Newton, his laws were mathematically verifiable with their data. To do this he had to invent a new complex mathematics: calculus. When the *Principia* was published, Isaac Newton was the Lucasian Professor at Cambridge University, a much valued position he assumed at the age of 28 after an astonishing ascension up the academic ladder. Stephen Hawking, generally regarded as the most brilliant theoretical physicist since Einstein, has held this post for the past two decades. While leading scientists of his day quickly recognized and understood Newton's laws and mathematics, they were difficult for many to grasp. On seeing Newton on the Cambridge campus, a student is reported to have said to his colleague "there goes a man who has written a book that even he doesn't understand." Early in his career Newton was quite introverted and worked alone with the help of an assistant. To my surprise, he spent much time studying alchemy.[5] He had an unusual interest in blood, and his favorite color was red. Newton was not a pleasant man. He was single-minded, was vindictive, was defensive, and carried on bitter disputes with other scientists.

Newton's laws define velocity and acceleration, as well as the concept of mass, force, and gravity. Set in mathematical form they provide direct proof of their validity through precisely and accurately predicting the orbits of planets and the paths and rates of projectiles. The two major contributions of the *Principia* were the laws of motion and the calculus, but it also contains a third important concept: fluid viscosity. Newton clearly saw that the forces necessary to move a fluid were directly proportional to the fluid's velocity gradients. This force is called shear stress, the proportionality constant is the fluid viscosity, the law is referred to as Newton's law of shear, and a fluid that follows this law is appropriately called a Newtonian fluid. Fig 1 is a schematic that illustrates how fluid shear stress at a point on a vessel wall, or wall shear stress, is defined. The velocity gradient is the reciprocal of the slope of the velocity profile near the wall. In calculus terms this is the first derivative of the velocity near the wall with respect to the radial distance from the wall. Newton's concept of a derivative is to let a finite gradient, such as $\Delta V/\Delta R$ in Fig 1, become infinitely small. Thus, in theory, if the differential equations that represent Newton's laws can be solved for the velocities, then the velocities and shear stresses are known for all locations and times in the flowing fluid. However, as illustrated later, there are only a few simple arterial geometries where the complex partial differential equations that describe fluid flow can be solved with classical mathematics. However, with one step backwards from the calculus infinitesimal to the finite precursors (such as $\Delta V/\Delta R$ in Fig 1), differential equations can be replaced by difference equations. Difference equations are solved by algebraic methods not by integration, a totally different and much simpler situation. Although all three of Newton's contributions, the laws of motion, calculus, and the fluid shear law, play a major role in the modern analysis of blood flow in arteries, it would be several centuries before the pieces were correctly assembled.

Wall Shear Stress = Viscosity (μ) $\times$ Velocity Gradient ($\Delta V/\Delta R$)

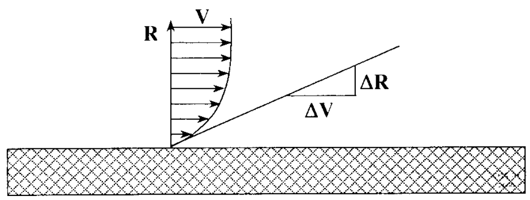

Fig 1. Newton's law of shear states that shearing forces (shear stress) are equal to the fluid's viscosity times the spatial velocity gradient. In this schematic illustrating fluid shear stress on the wall, the spatial velocity gradient is $\Delta V/\Delta R$ where V is velocity and R is radial distance from wall. In the fluid away from the wall, fluid shear stress approaches zero as $\Delta V/\Delta R$ becomes small.

THE 18TH CENTURY: HALES AND BERNOULLI

Stephen Hales (1677-1761) was an ordained minister with no formal medical education but an interest in science. He postulated that "the all-wise Creator has observed the most exact proportions of number, weight and measure in the make of all things." Hales was the first to measure arterial blood pressure.[1,3] He cannulated the carotid artery of a horse with a brass tube connected to a vertical glass tube and recorded a mean pressure of 9 ft 6 in of blood (approximately 220 mm Hg). He then successively hemorrhaged the animal to death at which time the carotid artery pressure was 2 ft (approximately 44 mm Hg). He recognized the elastic capacity of the arterial tree and its importance in propagating flow during diastole. Hales formulated a concept of peripheral vascular resistance based on small "capillary arteries" not visible to the eye. Encouraged by Newton, who was the president of The Royal Society of London in the early part of the 18th century, Hales published his work in several books, which became classics.

Daniel Bernoulli (1700-1782) was a physician who was strongly influenced by his father and uncle, both famous mathematicians and physicists.[6] He formulated and demonstrated the principles of conservation of energy in fluids. His book *Hemodynamica*, published in 1738, established Bernoulli's law, which states that along streamlines in a flowing fluid the sum of the pressure energy, the kinetic energy, and the gravitational energy (height) is constant.[6] However, it remained for his friend Leonhard Euler to put this in mathematical terms. Although Bernoulli's law has been frequently applied to arterial blood flow problems, it is missing a major term, the energy lost or dissipated by the viscous forces. He neglected that which Newton considered a major force, the viscosity. This means that the Bernoulli equation is applicable only to fluids of zero viscosity, so-called perfect fluids. The shear stresses, pressure drops, and energy dissipated because of viscous forces are neglected. This is at variance with observed facts and is hardly an adequate way to study or model arterial blood flow except in special simplified situations. Later, the viscous energy loss term was added as an unknown fudge factor to be measured experimentally or estimated. This formulation is currently referred to as the modified Bernoulli equation, primarily of use in the field of hydraulics where the fudge factors are known.

The complete three-dimensional differential equations that accurately describe fluid flow including the viscous terms were set down independently by Navier in 1817 and by Stokes in 1845.[6] The Navier-Stokes equations are basically Newton's laws of motion and viscosity applied to a flowing fluid. Because they are complex, partial differential equations, they are only mathematically solvable in highly simplified vessel geometric and flow situations. This roadblock to understanding arterial blood flow in realistic arterial geometries has only recently been bypassed by computational analysis with large high-speed computers.

THE 19TH CENTURY: POISEUILLE AND YOUNG

Jean Leonard Marie Poiseuille (1799-1869) studied physics and mathematics in Paris and transferred to medical school. For his doctoral thesis in 1828, he devised a mercury manometer and showed that the pressure in the aorta was approximately the same as the pressure in the smallest arterial branches. This confirmed Stephen Hales' deduction that the location of the pressure drop in the circulation, or the peripheral resistance, was in the very small–diameter blood vessels. He then set out to determine why. In 1840 Poiseuille published the findings that made him famous. He showed experimentally that for constant or steady flow in a straight round vessel, the pressure drop was directly proportional to the flow rate, to the viscosity, and to the vessel length, but was inversely proportional to the fourth power of the vessel radius. This is Poiseuille's law.[2] The observation of a highly nonlinear inverse relationship between pressure drop and vessel radius confirmed that the major resistance to blood flow in normal arterial systems is at the microcirculation or arteriolar level. Twenty years later in 1860, Gotthilf Hagenbach solved the newly proposed Navier-Stokes equations for steady flow in a round straight vessel confirming both Poiseuille's law and Newton's law of viscosity. The exact solution is $\Delta P = 8QL\mu/\Pi R^4$, where ΔP is the pressure drop, Q the flow rate, L the vessel length, μ the viscosity, and R the vessel radius. Another way to view this is that pressure drop equals resistance times flow, where resistance is $8\ L\mu/\Pi R^4$. The Hagen-Poiseuille equation predicts a parabolic velocity profile. The concept of vascular resistance for steady flow was later replaced by that of impedance for pulsatile flow. In 1883 Osborne Reynolds, while studying flow in pipes, described the transition from laminar flow (smooth like the Hagen-Poiseuille solution predicts) to turbulent flow (chaos or random inefficient fluid motion superimposed on forward flow). He determined that the critical dimensionless number for transition from laminar to turbulent flow is given by the vessel diameter times the mean velocity divided by viscosity. This is called the Reynolds number.[2,6] In general, arterial blood flow remains laminar except in regions of high-grade stenoses.

Like Poiseuille, Thomas Young (1773-1839) was a physician and a physicist. A multitalented man, he became famous for his studies of elasticity, including the properties of arteries that give them the ability to propagate both pressure and flow pulses. In his honor the proportionality constant for the relationship between load (stress) and deformation (strain) in solid elastic materials is called Young's modulus. He developed a theory of the perception of visual color based on red, green, and violet, assuming light followed the wave theory. In a later time Young would have been an invaluable intelligence officer because he deciphered the code of Egyptian hieroglyphics.

THE 20TH CENTURY: MCDONALD, WOMERSLEY, FRY, AND VASCULAR SURGEONS

The ability to measure both blood flow and blood pressure provided the opportunity for major advancements in further understanding arterial blood flow in human beings as well as its relationship to acquired and congenital vascular diseases. Donald McDonald (1917-1973) a physician and physiologist published the classic modern text on blood flow in arteries in 1960.[7] A second edition appeared in 1974[2] shortly after his death, followed by a third edition by William Milnor and Wilmer Nichols in 1990.[8] McDonald assembled a complete description of the many contributions to the understanding of arterial blood flow that had occurred since the turn of the century. I had the pleasure of knowing him during my surgical residence at the University of Alabama Medical Center in Birmingham. At the time I was studying the distribution of myocardial blood flow using radioactive microspheres. His advice and insight were always helpful and appreciated. Although McDonald's texts have served as a major reference for vascular researchers, the publication of *Hemodynamics for Surgeons* in 1975 by Gene Strandness and David Sumner brought a wealth of practical information to vascular surgeons in a comprehensible form.[9]

John Womersley (1907-1958) was a mathematician who worked with Donald McDonald for a short period and was motivated by him to investigate arterial blood flow. In 1955 Womersley published the solution to the Navier-Stokes equations for pulsatile flow in a straight round tube.[10] He defined a nondimensional number that characterizes pulsatile flow, the Womersley number. This was about 100 years after Hagen's solution of Poiseuille's flow problem for steady flow in a straight round tube. Hagen's and Womersley's solutions basically constitute the extent of the ability of classical mathematics to solve the equations of fluid flow. Although these solutions are helpful, they are too simple to be of much benefit in investigating realistic arterial circulatory problems.

The concept of the adverse effects of fluid shearing forces on arterial walls was probably first introduced by Donald Fry in 1957.[11] He showed that high wall shear stresses of 420 dyne/cm^2 produce histologic and biochemical changes in arterial endothelial cells. Subsequently it became clear that zones of low wall shear stress and high wall shear stress gradients were much more commonplace in normal and diseased arteries. These abnormal wall shear stresses and their gradients are produced by disturbed flow characterized by recirculation zones, flow separation and reattachment on walls, vortex formation with and without propagation, and prolonged near-wall residence times. Abnormal wall stresses in turn trigger a cascade of adverse biological events that may result in myointimal hyperplasia, atherosclerosis, thrombus formation, or arterial remodeling. Pathologic end points often develop at bifurcations, branch points, and anastomotic sites. Vascular surgeons who have made important contributions to understanding the role of adverse hemodynamics on arterial diseases include Chris Zarins, an honorary member of this Society. Bauer Sumpio, who did his vascular fellowship at the University of North Carolina with George Johnson, continues his groundbreaking research on the effects of flow-induced cyclic stresses and strains on endothelial biology. However, in vivo and in vitro experimental studies are limited in their ability to accurately measure flow in complex realistic arterial trees. Because accurate knowledge of near-wall blood flow is necessary to determine wall shear stresses and their gradients, some investigators have returned to the fundamental equations of fluid mechanics with a new yet old solution technique.

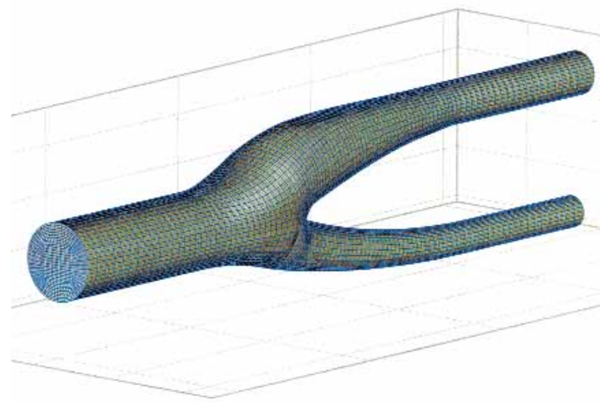

Fig 2. Three-dimensional carotid bifurcation that has been divided into 58,000 nodes or grids. Computational analysis gives solutions for pressures, velocities, and shear stresses, as well as their spatial and temporal gradients at each node. Grids as small as 60 µm in linear dimension can be used. (Unpublished computational analysis results of S. Hyun, C. Kleinstreuer, and J. P. Archie, 2000.)

COMPUTATIONAL ANALYSIS

Computational numerical methods have become the standard in almost every scientific field and industry where complex processes are governed by laws that can be represented by equations. For example, computational biology has been defined as the analysis and modeling of complex

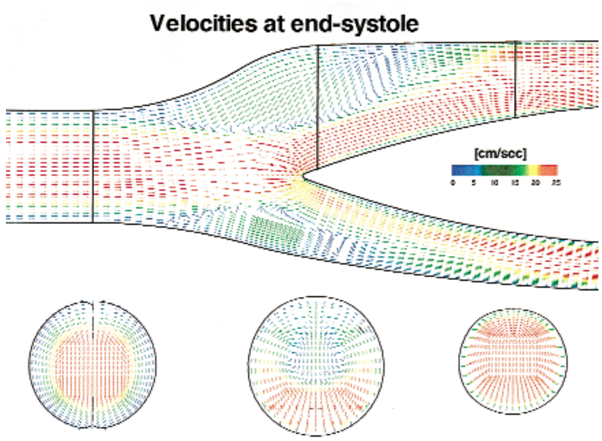

Fig 3. Color-coded mid-plane velocities at end systole are given in a carotid bifurcation. There are complex flow patterns throughout bulb segment. (Unpublished computational analysis results of S. Hyun, C. Kleinstreuer, and J. P. Archie, 2000.)

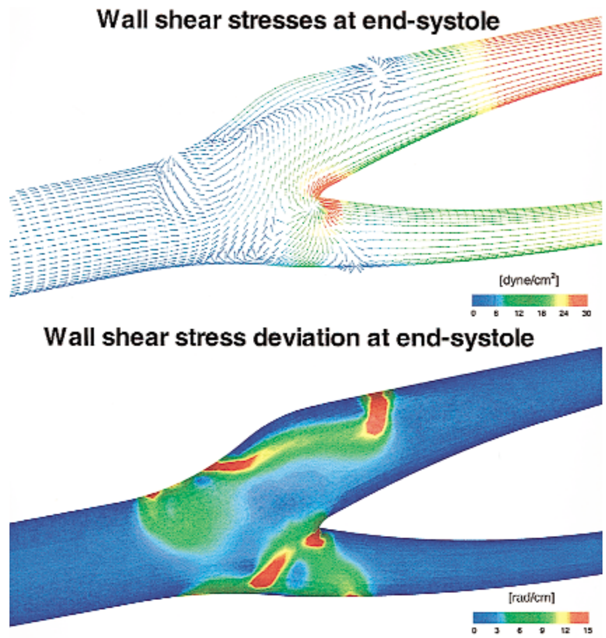

Fig 4. Color-coded wall shear stresses (*top*) and wall shear stress deviations or gradient (*bottom*) are given in carotid bifurcation at end systole. (Unpublished computational analysis results of S. Hyun, C. Kleinstreuer, and J. P. Archie, 2000.)

cellular, genetic, and molecular systems. The accuracy of these techniques is directly related to how well the equations describe the problem being studied. For arterial blood flow the match is excellent. For other problems of interest to vascular surgeons such as the structural and failure analysis of abdominal aortic aneurysms, the linear elasticity equations used currently do not accurately describe the complex nonhomogeneous and anisotropic aneurysm walls, nor do they account for the change in geometry from a normal aortic diameter. Classical mathematical methods have not and most likely will never solve the partial differential equations that describe complex physical and biological problems that occur in the real world.[12] Although the elliptical orbits of planets, moons, and satellites, the paths of projectiles, and the steady and pulsatile flow of blood in straight cylindrical tubes are examples of solvable problems, the quantitative analysis of blood flow in realistic arterial geometries is much more difficult. A different set of mathematical rules apply by going backwards one step from what constitutes a calculus derivative, which is an infinitesimal change in a dependent variable such as velocity with respect to an independent variable such as time or location, to a finite difference equation that is algebraic in form. In this process called *discretization,* differential equations are replaced by their corresponding difference equations and are subject to the rules of algebra, not those of calculus. Discretized algebraic equations can be solved numerically at a finite number of times and locations. In this way numerical methods are similar to in vitro or in vivo experimental studies. In computational analysis arterial lumens are represented by thousands of tiny nodes or grids that have common walls for a carotid bifurcation as illustrated in Fig 2. For an accurate computation of the blood flow in a typical three-dimensional bifurcating or branching artery, such as the carotid or infrarenal abdominal aorta, a mesh of 20,000 to 70,000 grid units is usually necessary. The discretized Navier-Stokes equations, now algebraic equations, that represent the fundamental physical laws of fluid mechanics are solved by repeatedly matching the values of the blood flow velocities and pressures at each adjacent grid wall or node.[12] There is a trade-off in the number of computer runs that are needed to reach numerical convergence of the equations for solutions at each grid and in the number of grid points. The finer the grid mesh, the larger the number of equations, but fewer computer runs are necessary. Twenty years ago super computers were needed to perform the millions of calculations necessary to solve even a simple arterial blood flow problem such as two-dimensional pulsatile flow in a branching artery.[13,14] Now, with parallel processing and other advancements, three-dimensional problems can be solved on in-house computers. To solve one of these with a handheld calculator or slide rule would take years, decades, or perhaps a lifetime.

The advantages of computational methods as compared with traditional laboratory or clinical research are (1) low cost, (2) speed, (3) complete information at all locations of interest, (4) simulation of realistic complex geometries, and finally and most important, (5) the ability to optimize the design.[12] The major potential disadvantage is that either the model equations or the geometry may not accurately represent the problem being investigated. For example, when arterial blood flow becomes turbulent, the classical Navier-Stokes equations break

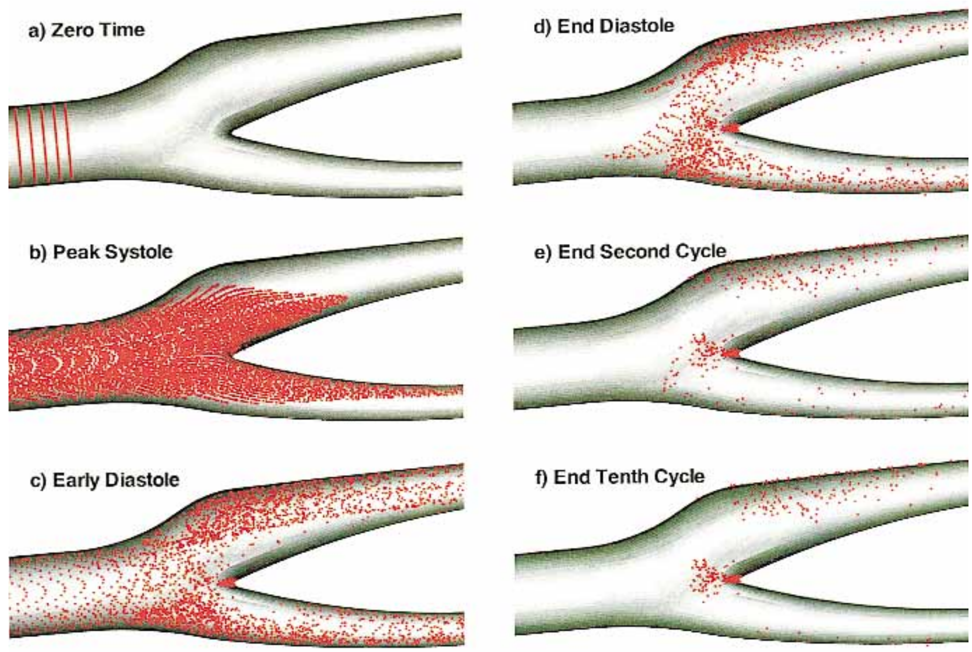

Fig 5. Computational analysis of particle deposition on the wall of a carotid bifurcation. At *top left* 15,000 microparticles are introduced into the distal common carotid artery. (Methodology from reference 15, unpublished figure.)

down because the energy losses due to turbulence are not accounted for. This means that for flow analysis in moderate-grade or high-grade stenotic lesions the equation must be modified to account for the Reynold's stresses, a project my colleague Clement Kleinstreuer at North Carolina State University is currently working on.

EXAMPLES OF COMPUTATIONAL SOLUTIONS

Blood flow has been studied in a number of bifurcating and branching arteries. These include the extracranial carotid, the celiac axis, and the aortic bifurcation. Examples of the distribution of velocities, wall shear stresses, and shear stress gradients in the three-dimensional carotid bifurcation of Fig 2 are given in Figs 3 and 4. In Fig 3 the color-coded velocities become low, stagnate, and reverse in the carotid bulb. This end-systolic example illustrates the most disturbed period of flow during the cardiac cycle. The velocities become more uniform at end diastole. In the upper section of Fig 4 there are zones of low wall shear stress in the bulb segment. However, it is the locations of high wall shear stress gradients or deviations, shown in the lower section of Fig 4, that may correlate with disease formation. An example of particle deposition on the wall of a carotid bifurcation is given in Fig 5.[15] Computational analyses such as these may help explain how and where blood components such as platelets, white cells, and lipids adhere to arterial walls.

The versatility of computational analysis is useful in a number of ways. Carotid endarterectomy reconstruction can be studied by optimizing the geometry to minimize wall shear stress gradients and, therefore, the possibility of myointimal hyperplasia formation.[13,14] Similarly, analysis of end-to-side graft to artery anastomosis indicates that hood-type reconstructions produce less disturbed flow and lower wall shear stress gradients than do standard and Taylor-patched geometries.[16] A recent analysis of stented arteries predicts low shear stress rates in the tiny canyons between stent wires and high rates near the leading edges of stent walls.[17] This near-wall information would be extremely difficult to obtain by direct measurements and may explain in part the early thrombogenic and myogenic nature of this intervention.

Another use of computational analysis for arterial blood flow is its application to in vivo arterial geometry. Both magnetic resonance and spiral computed tomography imaging can be used to generate or fit a mesh or grid network to the lumen of patients' normal or diseased arteries.[18] All that is needed to compute the flow velocities, shear stresses, and pressures is the inflow pulsatile waveform. It can be obtained with Doppler ultrasound. In this way a virtual vascular laboratory can analyze the effects or normal variations of arterial geometry on blood flow and possible adverse hemodynamics.[19]

SUMMARY

Mathematicians, engineers, physicians, and vascular surgeons have all contributed to understanding blood flow in arteries. The common thread has been the ability to measure or calculate blood flow and pressure. I was profoundly influenced by the requirement of quantitative, accurate, and precise measurements by both Julien Hoffman, who taught me basic vascular research, and John Kirklin, who taught me clinical research and the mental and technical skills necessary to operate effectively and efficiently. This is illustrated by the words of Lord Kelvin: "When you can measure what you are speaking about, and express it in numbers, you know something about it; but when you cannot measure it or express it in numbers, your knowledge is of a meager and unsatisfactory kind."

For me the history of arterial blood flow is best summarized by T. S. Eliot:

The dance along the artery
The circulation of the lymph
Are figured in the drift of the stars

(From "Burnt Norton," *Four Quartets*)

Although Isaac Newton's monumental gifts to mankind were derived to explain the drift of the stars, they also quantitatively predict the dance along the artery.

REFERENCES

1. Comroe JH Jr. Retrospectroscope: insights into medical discovery. Menlo Park (CA): Von Gehr Press; 1977.
2. McDonald DA. Blood flow in arteries. 2nd ed. Baltimore: Williams & Wilkins; 1974.
3. Fishman AP, Richards DW. Circulation of the blood: men and ideas. New York: Oxford University Press Inc; 1964.
4. Newton I. The principia. Motte A, translator. New York: Prometheus; 1995.
5. White M. Isaac Newton: the last sorcerer. Redding (MA): Perseus; 1997.
6. Smits AJ. A physical introduction to fluid mechanics. New York: John Wiley & Sons; 2000. p. 448-73.
7. McDonald DA. Blood flow in arteries. Baltimore: Williams & Wilkins; 1960.
8. Nichols WW, O'Rourke MF. McDonald's blood flow in arteries. Philadelphia: Lua & Febiger; 1990.
9. Strandness DE, Sumner DS. Hemodynamics for surgeons. New York: Grune & Statton; 1975.
10. Womersley JR. Method for the calculation of velocity, rate of flow and viscous drag in arteries when the pressure gradient is known. J Physiol 1955;127:553-62.
11. Fry DL. Acute vascular endothelial changes associated with increased blood velocity gradients. Circ Res 1967;22:165-97.
12. Patankar SV. Numerical heat transfer and fluid flow. New York: McGraw Hill; 1980.
13. Nazemi M, Kleinstreuer C, Archie JP. Pulsatile laminar flow and plaque formation in a carotid artery bifurcation. J Biomech 1990;23:1031-7.
14. Wells DR, Archie JP, Kleinstreuer C. The effect of carotid artery geometry on the magnitude and distribution of wall shear stress gradients. J Vasc Surg 1996;23:667-78.
15. Hyun S, Kleinstreuer C, Archie JP. Computer simulation and geometric design of endarterectomized carotid artery bifurcations. Crit Rev Biomed Eng 2000;28:53-9.
16. Lei M, Archie JP, Kleinstreuer C. Computational design of a bypass graft that minimizes wall shear stress gradients in the region of the distal anastomosis. J Vasc Surg 1997;25:637-46.
17. Berry JP, Santamarina A, Moore JE, Roychowdhury S, Routh WD. Experimental and computational flow evaluation of coronary stents. Ann Biomed Eng 2000;28:386-98.
18. Moore JA, Steinman DA, Holdsworth DW, Ethier CR. Accuracy of computational hemodynamics in complex arterial geometric reconstruction from magnetic resonance imaging. Ann Biomed Eng 1999;27:32-41.
19. Taylor CA, Hughes TJ, Zarins CK. Computational investigations in vascular disease. Computers in Physics 1996;10:224-32.

Submitted Jan 29, 2001; accepted Feb 1, 2001.